

2. NON-TECHNICAL ABSTRACT

There is no curative therapy for patients with androgen independent prostate cancer. The ability for vaccines to stimulate an immune response against cancer cells depends on the activity of specific T-cells, which can recognize a particular protein, or antigen, found on the tumor cells. These T-cells can be generated by immunization with poxviruses that contain the genes for the tumor proteins. The most commonly found protein in prostate tumor cells is PSA. Vaccinia virus is the vaccine used to prevent smallpox and has been used to produce the PSA protein previously. Fowlpox virus is a virus that infects birds but does not cause disease in humans and has also been used to produce the PSA protein. These vaccines, expressing multiple tumor antigens, have been tested in humans with cancer and appear to be safe after being given to over 600 people in clinical trials. The T-cells also require a second signal to become fully activated, which are provided by specialized immune system proteins called co-stimulatory molecules. There are many co-stimulatory molecules that have been discovered and can be used to help activate T-cells. A new vaccine has been developed using vaccinia virus to express PSA and three co-stimulatory molecules (called B7.1, ICAM-1, and LFA-3), called PROSTVAC-V. In addition, a new fowlpox virus was also made with the human PSA and three co-stimulatory molecule genes, and called PROSTVAC-F. Animal studies and at least two human clinical trials have suggested that the use of two different vaccines, such as vaccinia followed by fowlpox virus, are better than using a single virus vaccine. Granulocyte-macrophage colony stimulating factor (GM-CSF) is a protein of the immune system that is approved for use in humans to increase the number of white blood cells and has also shown some promise as an anti-cancer agent, especially when used in combination with vaccines. The goal of this study is to determine whether the prime/boost regimen of PROSTVAC-V followed by PROSTVAC-F in combination with GM-CSF is safe and effective and can stimulate an immune response against PSA on the prostate tumor cells.